In the United States Court of Federal Claims

No. 17-480V
Filed Under Seal: May 6, 2021
Reissued: June 14, 2021*

E.S., Petitioner, v. THE UNITED STATES, Respondent.	)	National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa–1 to –34; Human Papillomavirus Vaccine ("HPV"); Influenza Vaccine.

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MEMORANDUM OPINION AND ORDER

GRIGGSBY, Judge

I. INTRODUCTION

Petitioner, E.S., seeks review of the November 13, 2020, decision of the special master (the "November 13, 2020, Decision") denying her claim for compensation under the National Childhood Vaccine Injury Act ("Vaccine Act"), 42 U.S.C. § 300aa–1 to –34. For the reasons set forth below, the Court **DENIES** petitioner's motion for review of the special master's November 13, 2020, Decision and **SUSTAINS** the decision of the special master.

* This Memorandum Opinion and Order was originally filed under seal on May 6, 2021. ECF No. 136. The parties were given an opportunity to advise the Court of their views with respect to what information, if any, should be redacted from the Memorandum Opinion and Order. On June 14, 2021, petitioner filed a joint status report on behalf of the parties stating that the parties had no redactions to the Memorandum Opinion and Order. ECF No. 139. And so, the Court is reissuing its Memorandum Opinion and Order, dated May 6, 2021, as the public opinion.

II. FACTUAL AND PROCEDURAL BACKGROUND[1]

A. Factual Background

In this Vaccine Act case, petitioner, E.S., alleges that the human papillomavirus ("HPV") and Hepatitis A vaccines that she received on July 15, 2014, and the HPV and influenza ("flu") vaccines that she received on August 19, 2015, significantly aggravated her pre-existing type I diabetes ("T1D") and caused her to develop a variety of other conditions and symptoms, including headaches, narcolepsy, chronic fatigue syndrome ("CFS"), postural orthostatic tachycardia syndrome ("POTS"), small fiber neuropathy ("SFN") and a cardiac condition. Pet'r Mem. at 1, 9, 20-23. On November 13, 2020, the special master denied E.S.'s claim for compensation under the Vaccine Act. *See generally* November 13, 2020, Decision ("Dec.").

1. E.S.'s Medical History

E.S.'s medical history is discussed in detail in the special master's November 13, 2020, Decision and is summarized here. Dec. at 2-12.

E.S. was born on January 2, 1996, and she was diagnosed with T1D when she was five years old. Pet'r Ex. 1 at 1; Pet'r Ex. 19 at 65. E.S.'s medical record also demonstrates issues with persistent lower back pain, intermittent hematuria, flank pain, kidney stones, surgery for hemorrhagic right ovarian cyst, irregular menses, selective immunoglobulin A deficiency, and rheumatoid arthritis. Pet'r Ex. 19 at 48-50, 66-69; Pet'r Ex. 4 at 152; Pet'r Ex. 3 at 5; Pet'r Ex. 23 at 10. The medical record also shows that E.S. visited the emergency room several times in 2011 and 2012, for various reasons, including mid-sternal chest pain, weakness, shortness of breath, flank pain, and blood in her urine. Pet'r Ex. 17 at 198-204; Pet'r Ex. 4 at 152-196.

E.S. reported several health problems to a pediatrician in the months prior to her July 15, 2014, vaccinations. Pet'r Ex. 3 at 16. Specifically, E.S. complained of recurring headaches and a sore throat. *Id.* In September 2013, E.S. was also diagnosed with adenopathy and acute pharyngitis. *Id.* at 19. In March 2014, E.S. was diagnosed with a viral infection. *Id.* at 13-15.

[1] The facts recounted in this Memorandum Opinion and Order are taken from the petitioner's petition ("Pet'r Pet."); petitioner's motion for review ("Pet'r Mot. for Rev.") and the memorandum in support thereof ("Pet'r Mem."); petitioner's exhibits ("Pet'r Ex."); the Secretary's exhibits ("Resp't Ex.") and the special master's November 13, 2020, Decision ("Dec."). Except where otherwise noted, the facts recited herein are undisputed.

In addition, in April 2014, E.S. visited the emergency room, where testing showed that she had a high level of blood glucose for a diabetic and that she had glucose and ketones in her urine. Pet'r Ex. 4 at 118-20.

On July 15, 2014, E.S. visited Dr. Rebekah Lipstein and received the HPV and the Hepatitis A vaccines—the first set of vaccinations at issue in this case. Pet'r Ex. 3 at 2, 8-12. The medical record shows that E.S. had no immediate reaction to these vaccines. *Id.*

In the fall of 2014, E.S. began college at Villanova University. Pet'r Mem. at 4. On September 2, 2014, E.S. visited the university's student health center for treatment of increased blood sugar levels and a sore throat. Pet'r Ex. 14 at 88-90. At that time, E.S. tested positive for group A streptococcus and she was prescribed antibiotics. *Id.*

Over the next several weeks, E.S. visited the university's student health center on multiple occasions and she visited the emergency room on October 2, 2014, to report abnormally high glucose levels. *Id.* at 70, 84-87; Pet'r Ex. 9 at 3-12. E.S. also reported other medical issues during these visits, including headaches, sinus pressure, and nausea. *Id.*

On December 5, 2014, E.S. visited the emergency room to complain of constant vomiting and diarrhea. Pet'r Ex. 9 at 27-35. Over the next few weeks, E.S. also visited the university's student health center multiple times to report increased glucose levels, diarrhea, vomiting, and abdominal pain. *See, e.g.*, Pet'r Ex. 14 at 68-69; Pet'r Ex. 17 at 12-21, 102-105.

On December 11, 2014, E.S. presented to Dr. Keith Benkov, a gastroenterologist. Pet'r Ex. 11 at 1-2. Later in December, E.S. was hospitalized after complaining about persistent headaches. Pet'r Ex. 17 at 97. Testing at that time showed that E.S. had elevated liver enzymes and possibly an enlarged liver. *Id.* at 15, 113. And so, Dr. Benkov concluded that E.S. had poor diabetic control, poor gastric emptying, and a fatty liver. *Id.* at 105. E.S. subsequently visited the emergency room to receive treatment for right flank pain, nausea, and vomiting on May 1, 2015. Pet'r Ex. 9 at 54.

On August 15, 2015, E.S. received the flu vaccine and her second dose of the HPV vaccine—the second set of vaccinations at issue in this case. Pet'r Ex. 3 at 5-7. During the subsequent fall of 2015 and early 2016, E.S. sought emergency medical care on a regular basis,

seeking treatment for complications with diabetes. *See generally* Pet'r Ex. 12; *see also* Pet'r Ex. 7 at 1-29; Pet'r Ex. 9 at 79-126.

Specifically, on October 10, 2015, and October 21, 2015, E.S. visited the emergency room. Pet'r Ex. 9 at 79-99; Pet'r Ex. 12 at 1. In December 2015, E.S. was diagnosed with hypokalemia. Pet'r Ex. 9 at 109.

In early 2016, E.S. sought treatment for chest pain from Dr. David Lefkowitz, a cardiologist. Pet'r Ex. 5 at 1-4. During her visit with Dr. Lefkowitz, E.S. reported that she had felt poorly since receiving the HPV vaccine, two other vaccines, and a tuberculosis skin test. *Id.* at 1.

In February 2016, E.S. visited Dr. Benkov, who found that her condition "could be some form of pancreatitis" and instructed E.S. to double her current dose of Protonix. Pet'r Ex. 11 at 1-2. In March 2016, E.S. took a leave of absence from Villanova University. Pet'r Ex. 24 at 6.

On May 12, 2016, E.S. visited Dr. Edith Schussler for an immune dysfunction consultation. Pet'r Ex. 23 at 5-8. During this consultation, Dr. Schussler concluded that E.S. did not appear to be a vaccine "non-responder" and that she should continue to be vaccinated. *Id.* at 13.

In May 2016, E.S. also visited Dr. John Wells for a neurologic evaluation. Pet'r Ex. 24 at 6-7. Dr. Wells concluded that E.S. had persistent headaches despite a normal neurological exam and a normal brain MRI/MRA. *Id.* at 7. And so, he recommended that E.S. follow up with her cardiologist and endocrinologist and try therapy for her anxiety. *Id.*

In August 2016, E.S. followed up with Dr. Wallach, an endocrinologist, who noted that E.S. could safely return to school. Pet'r Ex. 19 at 2. Thereafter, in October 2016, E.S. obtained mental health counseling. Pet'r Ex. 13 at 5-6. E.S. also visited Dr. Sanjeev Kothare for evaluation of possible seizures and sleep problems. Pet'r Ex. 22 at 5.

The medical record shows that E.S.'s visit with Dr. Kothare is the first time that E.S. reported daytime sleepiness, insomnia, sleep paralysis, vivid/violent dreams, panic attacks, and depressed mood, all of which E.S. attributed to the flu vaccine that she received on August 19, 2015. *Id.*; *see also* Pet'r Ex. 1 at 3. Dr. Kothare performed a variety of tests and ultimately

diagnosed E.S. with narcolepsy type 2, non-REM parasomnia, and REM sleep disorder. Pet'r Ex. 22 at 9.

In October 2016, laboratory results confirmed that E.S. was positive for anti α-1-adrenergic antibodies and anti-muscarinic cholinergic receptor 4 antibodies and that she was "at risk" for anti-muscarinic cholinergic receptor 3 antibodies. Pet'r Ex. 16 at 1.

In November 2016, E.S. underwent a nocturnal polysomnography test, which revealed the existence of mild sleep apnea and "upper airway resistance syndrome." *Id.* at 26-27. In early 2017, E.S. took a multiple sleep latency test, which revealed "evidence of excessive daytime sleepiness," which "could be consistent with narcolepsy under the appropriate clinical circumstances[.]" Pet'r Ex. 36 at 33, 35.

On February 23, 2017, E.S. again visited Dr. Lefkowitz, who expressed the view that E.S.'s potentially cardiac-associated symptoms were not likely the product of coronary disease and that they were likely associated with her diabetes. *See* Pet'r Ex. 18 at 14.

In May 2017, E.S. visited the emergency room for chest pain and she was diagnosed at that time with non-specific chest pain and hypoglycemia. Pet'r Ex. 33 at 65. E.S. returned to the emergency room four days later due to issues with her insulin pump and due to chest pain, and she was diagnosed at that time with hypoglycemia and nausea. *Id.* at 11.

In January 2018, E.S. returned to the emergency room and she reported abdominal, rectal, and chest pain with nausea. Pet'r Ex. 34 at 1. E.S. also sought treatment in April 2018 for sleep issues. Pet'r Ex. 102 at 1.

Dr. Alcibiades J. Rodriguez, a sleep medicine specialist, recommended that E.S. take Clonazepam and that she follow up in three months. *Id.* In June 2018, E.S. visited Dr. Susan Levine, who assessed E.S. with inflammatory neuropathy, autonomic dysfunction, gastroparesis, and endometriosis. Pet'r Ex. 98 at 27. E.S. followed up with Dr. Levine in August 2018, and Dr. Levine assessed E.S. with having, among other things, ME/CFS, post-HPV vaccine onset of CFS symptoms, dysautonomia, and POTS. *Id.* at 26.

In the fall of 2018, E.S. visited Dr. Russell Chin, a neurologist. Pet'r Ex. 48 at 1; Pet'r Ex. 49 at 1. Dr. Chin expressed the view that E.S.'s concerns about intermittent tingling sensations in her mid-chest region and the "chilled" sensations to her scalp, neck, and shoulders

were likely attributable to her other dysautonomic/autoimmune issues, but that the "[e]tiology of these symptoms is unknown." Pet'r Ex. 49 at 7. Testing at that time also revealed that E.S. had reduced sweat gland nerve fiber density, which was consistent with SFN. Pet'r Ex. 48 at 1.

Most recently, E.S. visited Dr. David S. Younger, a neurologist, on August 12, 2019, and November 7, 2019. Pet'r Ex. 105 at 3. Dr. Younger's examinations showed, among other things, sensory loss, hyporeflexia, distal leg weakness, Romberg sign, and tandem imbalance. *Id.* And so, he recommended additional screening and a psychiatric assessment. *Id.* at 5, 6.

2. The Expert Reports

E.S. and the Secretary both rely upon several experts to address E.S.'s vaccine injury claims. First, E.S. submitted reports prepared by three experts—Dr. Lawrence Steinman, Dr. Sin Hang Lee and Dr. Susan Levine.[2] The Secretary also submitted reports prepared by four experts—Dr. Shane LaRue, Dr. Andrew MacGinnitie, Dr. David Raizen and Dr. Christopher Gibbons.

With regards to E.S.'s experts, Dr. Laurence Steinman is a professor in the departments of neurology, pediatrics, and genetics at Stanford University. Pet'r Ex. 40 at 1. In his first expert report, Dr. Steinman opined that E.S.'s narcolepsy could have been caused by the HPV vaccine. Pet'r Ex. 39 at 6-27. In this regard, Dr. Steinman cited the *L. Arnheim-Dahlstrom* study, which shows evidence of an increased rate of narcolepsy in test subjects immunized with the HPV vaccine. Pet'r Ex. 39, reference 24 at 8. Dr. Steinman also observed that decreased levels of hypocretin and/or abnormalities in hypocretin receptor 2 in the brain are scientifically understood to play a role in the occurrence of narcolepsy and that aberrant immune responses are thought to possibly explain such circumstances. Pet'r Ex. 39 at 8 (citing Pet'r Ex. 39, references 9 and 10).

[2] Petitioner also submitted numerous medical articles and case studies to support her theory that the HPV vaccine can cause POTS. *See, e.g.*, Pet'r Ex. 108 (*Del Pozzi* study regarding an 18-year-old female who developed POTS after receiving the HPV vaccine); Pet'r Ex.109 (*Gunning* study noting that POTS may be an autoimmune disorder). But, petitioner has never been diagnosed with POTS. Pet'r Sur-Reply at 3 ("Petitioner . . . has not relied on a diagnosis of [POTS]. Petitioner's case is not predicated on a POTS diagnosis, even though Dr. Younger's medical record and testing points in the direction of a POTS diagnosis. More testing may well establish a POTS diagnosis . . . .").

Dr. Steinman similarly opined that the HPV vaccine could plausibly trigger an autoimmune cross-reaction sufficient to produce headaches. *Id.* at 27-30. To support this theory, Dr. Steinman cited numerous medical articles and case studies, including the *Obermann* review and the *Khan* study. Pet'r Ex. 39, reference 26 at 4 (*Obermann* review implying that calcitonin-gene-related-peptide is involved in migraines); Pet'r Ex. 39, reference 27 at 1 (*Khan* study showing that alum in the HPV vaccine persisted for a year in animal models and may cause chronic side effects); *see also* Pet'r Ex. 39, reference 7 at 1 (HPV vaccine package insert noting that headache is the most common adverse reaction to the HPV vaccine). And so, Dr. Steinman concluded that E.S.'s narcolepsy and headaches could plausibly have been caused by the HPV vaccine. Pet'r Ex. 39 at 31.

In addition, Dr. Steinman expressed the view that the antibodies that were found at elevated levels in some CFS patients could be produced as part of an autoimmune, cross-reactive process instigated by the HPV vaccine. Pet'r Ex. 86 at 24-26. To support this theory, Dr. Steinman cited numerous medical articles and case studies, including the *Blitshteyn*, *Loebel* and *Ikeda* studies. Pet'r Ex. 96 at 4 (*Blitshteyn* study noting that elevated muscarinic receptor 3 and 4 antibodies have been found in CFS patients); Pet'r Ex. 97 at 1 (*Loebel* study noting that antibodies against M3 and M4 receptors were significantly elevated in CFS patients compared to controls); Pet'r Ex. 107 at 4 (*Ikeda* study noting that the autoantibodies against the adrenergic receptor β2 and muscarinic acetycholine receptor 3 and 4 were significantly elevated in the serum of patients with CFS). Dr. Steinman also relied upon the results of his searches on the Basic Local Alignment Search Tool ("BLAST") —a medical/scientific internet resource—to support petitioner's medical theory. *See, e.g.*, Pet'r Ex. 39 at 9, 11-21, 28-29; Pet'r Ex. 86 at 1-4, 16-18, 27-34. And so, Dr. Steinman concluded that the HPV vaccine is likely to have caused E.S.'s CFS, headaches and narcolepsy. Pet'r Ex. 86 at 38.

Lastly, Dr. Steinman opined that the onset of E.S.'s CFS and SFN were medically-acceptable, because E.S. experienced overlapping symptoms from the HPV vaccine and some weeks and months were needed for antibody development to eventuate in clinical symptoms. Pet'r Ex. 99 at 1. In support of this conclusion, Dr. Steinman cited an observational study from Japan showing that certain symptoms, including fatigue, headache, sleep disturbance, and

autonomic dysfunction, manifested on average within 360 days of the subject receiving the HPV vaccine. *Id.* at 2 (citing Pet'r Ex. 100).[3]

E.S.'s second expert, Dr. Sin Hang Lee, is currently the director of the Milford Molecular Diagnostics Laboratory in Milford, Connecticut. Pet'r Ex. 42 at 2. Dr. Lee opined that the HPV vaccine exacerbated E.S.'s T1D. Pet'r Ex. 41 at 4-6. In this regard, Dr. Lee noted that the clinical trials of the HPV vaccine showed that two vaccinated individuals reported new cases of T1D. *Id.*

Dr. Lee also opined that the HPV vaccine could trigger a myocardial ischemia due to low blood perfusion and that the HPV vaccine was the most probable cause of E.S.'s myocardial ischemia. *Id.* at 15, 17-18. Finally, Dr. Lee opined that the onset of E.S.'s symptoms was medically-acceptable, because: (1) the timing of the exacerbation of E.S.'s T1D is consistent with the timeframe that the HPV vaccine manufacturer reported for subclinical T1D to become overt clinical diabetes and (2) the timing of the discovery of E.S.'s myocardial ischemia symptoms is consistent with the CDC's post-licensure safety surveillance analysis on the HPV vaccine. *Id.* at 14, 18.

Lastly, Dr. Susan Levine, a board-certified specialist in infectious diseases, submitted a one-page letter in support of E.S.'s claim, in which she opined that E.S. suffers from CFS, orthostatic intolerance, "brain fog," and migraine headaches. Pet'r Ex. 47 at 1.

With regards to the Secretary's experts, Dr. Shane LaRue is a cardiologist, who opined that there was little evidence to support the conclusion that E.S. suffered from any meaningful form of cardiac issue. Resp't Ex. A at 5. In addition, Dr. LaRue opined that none of the vaccines that E.S. received could cause myocardial ischemia. *Id.* at 5-6.

Dr. Andrew MacGinnitie, a pediatrician and immunologist/allergist at Boston Children's Hospital, opined that "a plausible case" exists for the contention that a specific flu vaccine could trigger narcolepsy with cataplexy (type 1 narcolepsy). Resp't Ex. C at 1-2, 4. But, Dr. MacGinnitie observed that E.S. has been diagnosed with type 2 narcolepsy, which is not accompanied by cataplexy and is not believed to be autoimmune-driven. *Id.* at 4-5, 7. And so,

[3] Petitioner also cites the *Kinoshita* study, which found nerve pathology abnormalities in a small segment of test subjects that received the HPV vaccine. Pet'r Mem. at 23; Pet'r Ex. 111 at 10.

Dr. MacGinnitie questioned whether Dr. Steinman had properly established that E.S.'s narcolepsy could plausibly be caused by an autoimmune response to any of the vaccines at issue in this case. *Id.* at 5-6.

Dr. MacGinnitie also opined that it is unlikely that a causal connection exists between the HPV vaccine and E.S.'s narcolepsy, because there is no epidemiological evidence of an association between narcolepsy and the HPV vaccine. *Id.* at 11. Dr. MacGinnitie also observed that the evidence linking the vaccines to E.S.'s headaches was not convincing and that there was insufficient evidence to establish a connection between the vaccines and the development of E.S.'s myocardial ischemia, or E.S.'s worsened control of her T1D. *Id.* at 11-12, 14, 16-17.

In addition, Dr. MacGinnitie concluded that there is no causal connection between the vaccines and E.S.'s CFS, because, among other reasons, E.S.'s CFS diagnosis occurred more than four years after she received the first set of vaccinations at issue in this case. Resp't Ex. H at 12.

In addition, Dr. David Raizen, a neurologist and associate professor at the University of Pennsylvania's medical school, opined that the findings that supported E.S.'s narcolepsy diagnosis had no relevance in establishing causation between the vaccines at issue and the diagnosis. Resp't Ex. E at 1, 7-8. Dr. Raizen also disputed whether there was any overlap between E.S.'s symptom of "unrefreshing sleep" and her narcolepsy diagnosis. Resp't Ex. I at 1-2. And so, Dr. Raizen concluded that E.S. had not shown that the HPV vaccine can be associated with chronic fatigue. *Id.* at 5.

Lastly, Dr. Christopher Gibbons, a board-certified neurologist and an associate professor of neurology at Harvard Medical School, opined that the medical record did not provide sufficient evidence to support E.S.'s SFN diagnosis. Resp't Ex. J at 1, 4-7.

The Secretary also submitted medical literature to the special master, including several articles to support the position that the vaccines at issue could not have caused the conditions alleged by E.S., or significantly aggravated E.S.'s T1D. *See generally* Resp't Exs. L, M, N.

After the Secretary moved to dismiss E.S.'s vaccine injury claims on September 13, 2019, and the parties fully briefed the issues raised in the Secretary's motion to dismiss, the

special master resolved the case without holding an evidentiary hearing. *See generally* Resp't Mot.; Dec.

3. The Special Master's Decision

On November 13, 2020, the special master issued a decision denying E.S.'s claim for compensation under the Vaccine Act. *See generally* Dec. As an initial matter, the special master observed in the November 13, 2020, Decision that several of the injuries alleged by the petitioner had not been preponderantly established. Dec. at 52-55. Specifically, the special master determined that the medical record shows that E.S. frequently sought medical treatment after the vaccinations at issue. *Id.* at 52. But, the special master also determined that many of E.S.'s medical conditions, other than complications attributable to her ongoing struggle with T1D, were not preponderantly supported by the medical record. *Id.* at 52-55.

In addition, the special master determined that petitioner's theories of causation in this case were unreliable and/or not preponderantly supported by the evidence. Dec. at 55-60. In this regard, the special master determined that E.S. failed to establish a causal connection between any of the vaccines at issue and her alleged injuries, for several reasons. *Id.* at 55.

First, with regards to E.S.'s claim that her POTS was caused by the vaccines, the special master observed that the Office of Special Masters has never found that causation exists between a vaccine and a POTS diagnosis. *Id.* at 56. The special master also determined that petitioner failed to provide reliable evidence supporting the conclusion that the HPV vaccine might cause POTS. *Id.* at 57-58.

In this regard, the special master observed that Dr. Steinman "makes the same literal arguments about theoretical homology between components of the HPV vaccine and muscarinic receptors that are always presented in such cases—but with insufficient reliable corroborative proof supporting the conclusion that the homology is *meaningful* from a pathogenic sense." *Id.* at 57 (emphasis in original). The special master further observed that "[e]stablishing the existence of potential homology based on internet-driven research performed solely for this case is not enough to meet the preponderant burden of establishing it more likely than not that the vaccine *would* cross-react as proposed." *Id.* (emphasis in original). And so, the special master concluded that E.S.'s "[a]rguments about the autoimmune character of POTS, or the possibility

that the HPV [v]accine could encourage the production of autoantibodies thought to be POTS-associated, were also unreliably established." *Id.*

Second, with regards to E.S.'s claim that her narcolepsy was caused by any of the vaccines at issue, the special master observed that prior attempts to establish causation between narcolepsy and the version of the flu vaccine widely used in the United States had failed in cases before the Office of Special Masters. *Id.* at 58. And so, he concluded that E.S.'s arguments that the flu vaccine could have caused her narcolepsy diagnosis were weaker than those rejected in *D'Toile*, a prior case. *Id.* (citing *D'Toile v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), *mot. for review den'd*, 132 Fed. Cl. 421 (2017), *aff'd*, 726 F. App'x 809 (Fed. Cir. 2018)). The special master also concluded that E.S.'s argument that the HPV vaccine can cause type II narcolepsy "was woefully unsupported with reliable proof." *Id.*

Third, the special master also rejected E.S.'s claim that her CFS was caused by the HPV vaccine, although he determined that E.S. was "on slightly more firm ground" in arguing that the HPV vaccination can cause CFS. *Id.* at 58-59. Specifically, the special master determined that E.S. did not present reliable scientific evidence showing that there is a likely connection between the HPV vaccine and CFS, for many of the same reasons that petitioner failed to establish a link between POTS and the vaccinations. *Id.* at 59. The special master similarly determined that E.S. had not shown that her SFN was caused by the HPV vaccine, because the methods used to establish that some homology exists between amino acid sequences in the HPV vaccine components and nerve cells were not adequate to establish a preponderant showing that the HPV vaccine can cause SFN. *Id.* In this regard, the special master observed that "merely showing via BLAST searches that some homology exists between amnio acid sequences in the HPV vaccine components and nerve cells" was not sufficient to satisfy the preponderance of the evidence standard. *Id.*

Fourth, the special master also determined that the medical record did not support a finding that E.S. experienced any of her alleged injuries in a medically-acceptable timeframe following the vaccinations at issue. *Id.* at 60. Notably, the special master determined that E.S. relied upon diagnoses made in 2016 and 2018—long after the vaccinations at issue here—to show causation. *Id.*; *see* Pet'r Ex. 22 at 9; Ex. 48 at 1; Pet'r Ex. 98 at 26.

In addition, the special master determined that E.S.'s preexisting diabetes has not been shown to have been exacerbated by any of the vaccines at issue in this case. Dec. at 61-64. In this regard, the special master observed that the Office of Special Masters has repeatedly determined that vaccination does not likely worsen T1D. *Id*. at 62. Nonetheless, the special master determined that, even if he ignored these prior cases, E.S. had not established that the HPV vaccine could worsen T1D. *Id*. In this regard, the special master observed that there was no evidence in the medical record to show that E.S. experienced a reaction to the first dose of the HPV vaccine prior to her hospital visit in October 2014. *Id*. at 63. The special master also observed that no treaters who saw E.S. "at any time close" to her receipt of first dose of the HPV vaccine opined that there could be a relationship between the vaccine and her T1D flares. *Id*. And so, the special master concluded that E.S. failed to show that her T1D aggravation occurred within a medically-acceptable timeframe. *Id.*

Lastly, the special master found E.S.'s experts to be either unpersuasive, or to offer unreliable opinions in this case. *Id*. at 64. Notably, the special master determined that Dr. Steinman's opinion was "frequently conclusory or unconcerned with its unreliability." *Id*. at 65. The special master also observed that Dr. Lee was not an immunologist, cardiologist or trained in the treatment or analysis of diabetes. *Id*. Given this, the special master afforded the opinions of these experts limited weight. *See id*. at 64-66. And so, the special master concluded that the overall picture in this case was unsupportive of the conclusion that any of the vaccines at issue were causal of ES.'s post-vaccination symptoms and he denied compensation in this case. *Id*. at 67-68.

E.S., alleging error, seeks review of the special master's decision.

B. Procedural Background

On December 14, 2020, E.S. filed a motion for review of the special master's November 13, 2020, Decision. *See generally* Pet'r Mot. for Rev. On January 11, 2021, the Secretary filed a response and opposition to the motion for review. *See generally* Resp't Resp.

The motion for review having been fully briefed, the Court resolves the pending motion.

III. LEGAL STANDARDS

A. Vaccine Act Claims

The United States Court of Federal Claims possesses jurisdiction to review the record of the proceedings before a special master and, upon such review, may:

> (A) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision,
>
> (B) set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law, or
>
> (C) remand the petition to the special master for further action in accordance with the court's direction.

42 U.S.C. § 300aa–12(e)(2).

The special master's determinations of law are reviewed *de novo*. *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010). The special master's findings of fact are reviewed for clear error. *Id.* (citation omitted); *see also Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1345 (Fed. Cir. 2010) ("We uphold the special master's findings of fact unless they are arbitrary or capricious."). The special master's discretionary rulings are reviewed for abuse of discretion. *Munn v. Sec'y of Dep't of Health & Hum. Servs.*, 970 F.2d 863, 870 n.10 (Fed. Cir. 1992).

In addition, a special master's findings regarding the probative value of the evidence and the credibility of witnesses will not be disturbed so long as they are "supported by substantial evidence." *Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349, 1355 (Fed. Cir. 2010) (citation omitted); *see also Burns v. Sec'y of Dep't of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (holding that the decision of whether to afford greater weight to contemporaneous medical records or later given testimony is "uniquely within the purview of the special master"); s*ee also Hibbard v. Sec'y of Health & Hum. Servs.*, 698 F.3d 1355, 1363 (Fed. Cir. 2012) (citation omitted) (stating that there is no reversable error so long as the special master considers relevant evidence, draws plausible inferences from said evidence, and articulates a rational basis for his decision.). This "level of deference is especially apt in a case in which the medical evidence of causation is in dispute." *Hodges v. Sec'y of Dep't of Health & Hum. Servs.*, 9 F.3d 958, 961

(Fed. Cir. 1993). And so, the Court will not substitute its judgment for that of the special master, "if the special master has considered all relevant factors, and has made no clear error of judgment." *Lonergan v. Sec'y of Dep't of Health & Hum. Servs.*, 27 Fed. Cl. 579, 579-80 (1993).

The United States Court of Appeals for the Federal Circuit has also recognized the probative value of the opinions of treating physicians contained in contemporaneous medical records. *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006). Such opinions and medical records are favored in Vaccine Act matters, because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id*. (quoting *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1280 (Fed. Cir. 2005) (brackets existing). But, these opinions are not "binding on the special master or court." 42 U.S.C. § 300aa–13(b)(1); *see also Snyder ex rel. Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 745 n.67 (citing *Andreu ex rel. Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1375 (Fed. Cir. 2009)) ("[T]here is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted."). Rather, "the special master or court shall consider the entire record and the course of the injury" when "evaluating the weight to be afforded to any such" opinion. 42 U.S.C. § 300aa–13(b)(1).

Under the Vaccine Act, the Court must award compensation if a petitioner proves, by a preponderance of the evidence, all the elements set forth in in 42 U.S.C. § 300aa–11(c)(1), unless there is a preponderance of evidence that the illness is due to factors unrelated to the administration of the vaccine. 42 U.S.C. § 300aa–13(a)(1). A petitioner can recover either by proving an injury listed on the Vaccine Injury Table (the "Table"), or by proving causation-in-fact. *See* 42 U.S.C. §§ 300aa–11(c)(1)(C)(i)-(ii); *Althen*, 418 F.3d at 1278. And so, to receive compensation under the National Vaccine Injury Compensation Program, a petitioner must prove either that: (1) the petitioner suffered a "Table Injury" that corresponds to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) petitioner's injury was actually caused by a vaccine. *See* 42 U.S.C. §§ 300aa–11(c)(1)(C)(i)-(ii), 300aa–14(a); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano*, 440 F.3d at 1319-20.

In addition, in Table and non-Table cases, a petitioner bears "a preponderance of the evidence" burden of proof. 42 U.S.C. § 300aa–13(a)(1)(A); *Althen*, 418 F.3d at 1278 (citing *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)). And so, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the [judge] of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2 (brackets existing) (citations omitted); *see also Snowbank Enters., Inc. v. United States*, 6 Cl. Ct. 476, 486 (1984) (holding that mere conjecture or speculation is insufficient under a preponderance standard).

In *Althen*, the United States Court of Appeals for the Federal Circuit addressed the three elements to prove causation-in-fact. *Althen*, 418 F.3d at 1278. To establish a *prima facie* case when proceeding on a causation-in-fact theory, a petitioner must "prove, by a preponderance of the evidence, that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface*, 165 F.3d at 1352.

In addition, a petitioner must prove by a preponderance of the evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278. In addition, all three elements "must cumulatively show that the vaccination was a 'but-for' cause of the harm, rather than just an insubstantial contributor in, or one among several possible causes of, the harm." *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). While the Vaccine Act does not require medical or scientific certainty, any theory posited must be "sound and reliable." *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (quoting *Knudsen by Knudsen v. Sec'y of Dep't of Health & Hum. Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994)).

The Vaccine Act defines significant aggravation as "any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." 42 U.S.C. § 300aa–33(4). In off-Table cases, like here, additional proof is necessary for a petitioner to prevail on a significant aggravation claim. 42 U.S.C. § 300aa-11(c)(1)(C).

In this regard, the Federal Circuit has held that to establish a prima facie case for the significant aggravation of an off-Table injury, a petitioner must show by preponderant proof that:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) . . . a proximate temporal relationship between the vaccination and the significant aggravation.

W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352, 1357 (Fed. Cir. 2013) (quoting *Loving ex. rel. Loving v. Sec'y of Health & Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009)). The Federal Circuit further makes clear that "a petitioner in an off-[T]able case must show the vaccine actually caused the significant aggravation—not just that, accepting petitioner's medical theory as sound, the person's condition worsened within a medically-acceptable time frame." *Id.*

Lastly, if a petitioner establishes a *prima facie* case, the burden shifts to the respondent to show, by a preponderance of the evidence, that the injury was caused by a factor unrelated to the vaccine. *See* 42 U.S.C. § 300aa–13(a)(1)(B); *see also Shalala v. Whitecotton*, 514 U.S. 268, 270-71 (1995). But, regardless of whether the burden of proof shifts to the respondent, the special master may consider the evidence presented by the respondent in determining whether the petitioner has established a *prima facie* case. *See Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case[-]in-chief.").

IV. LEGAL ANALYSIS

Petitioner raises two objections to the special master's November 13, 2020, Decision denying her Vaccine Act claim. First, petitioner argues that the special master's decision was rendered irrational by an internal inconsistency regarding whether the HPV vaccine significantly

aggravated her T1D and that the special master's interpretation of the medical record was arbitrary and capricious. Pet'r Mem. at 2. In this regard, petitioner contends that: (1) the special master reached conflicting conclusions about whether her T1D was under control prior to the receipt of the vaccinations at issue; (2) the special master abused his discretion by citing petitioner's behavior during late adolescence as diminishing evidence of causation; (3) the special master misconstrued the medical record regarding petitioner's SFN diagnosis; (4) the special master overly relied upon unrelated case law regarding an autoimmune connection between vaccination and SFN; (5) the special master heightened petitioner's burden of proof, by dismissing the significance of the establishment of homologies between the HPV vaccine amnio acid sequence and human nerve cells; (6) the special master arbitrarily determined that there is no link between CFS and the HPV vaccine; and (7) petitioner satisfied prongs 1, 2 and 3 of *Althen* with regards to her claim that the HPV vaccine caused her CFS. *Id*. at 16-24.

In addition, petitioner argues that the special master improperly heightened her burden of proof, by holding that older case law precludes a finding that a vaccine could cause T1D. *Id*. at 2, 24-26. And so, petitioner requests that the Court set aside the special master's November 13, 2020, Decision and remand this matter to the special master for a determination of compensation. *Id*. at 26.

The Secretary counters that the special master correctly determined that the evidentiary record in this matter does not support petitioner's claim that the vaccines at issue significantly aggravated her T1D, or caused her other injuries. Resp't Resp. at 9-19. In this regard, the Secretary argues that: (1) the special master's determinations regarding petitioner's medical diagnoses are immaterial to the decision to deny compensation in this case; (2) petitioner fails to identify any reversible error related to the special master's findings regarding causation and a temporal relationship; (3) any inconsistency in the special master's decision regarding the worsening of petitioner's T1D was harmless error; and (4) the special master appropriately considered prior case law in analyzing petitioner's claim. *Id*. And so, the Secretary requests that the Court deny petitioner's motion for review and sustain the decision of the special master. *Id.* at 19-20.

For the reasons discussed below, the evidentiary record in this case shows that the special master did not abuse his discretion, or act contrary to law, in reaching the decision to deny

petitioner's Vaccine Act claim. And so, the Court **DENIES** petitioner's motion for review of the special master's November 13, 2020, Decision and **SUSTAINS** the decision of the special master.

A. The Special Master's Comment Regarding Petitioner's Pre-Vaccination Control Of Her T1D Was A Harmless Error

As an initial matter, to the extent that the special master made inconsistent statements about the level of petitioner's control of her T1D prior to receiving the vaccinations at issue in this case, this error was harmless. In her motion for review, petitioner correctly observes that the special master states in the November 13, 2020, Decision that petitioner had "good control" of her T1D prior to receiving the vaccinations at issue and that the special master also states that "petitioner's diabetes was not under fair control prior to vaccination." Pet'r Mem. at 17-18 (quoting Dec. at 2, 62 n.78) (emphasis omitted). But, a careful review of the November 13, 2020, Decision also makes clear that the special master acknowledged and accepted that petitioner's "overall health declined post-vaccination—satisfying the third *Loving* prong." Dec. at 62; *Loving ex. rel. Loving v. Sec'y of Health & Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009). Given this, the special master's analysis of petitioner's significant aggravation claim was not impacted by his varying statements about the level of petitioner's control of her T1D prior to the vaccinations. Dec. at 62.

The November 13, 2020, Decision also makes clear that the special master rejected petitioner's significant aggravation claim, because he determined that petitioner had not established that the HPV vaccine (or any other vaccine) was responsible for the acknowledged worsening of her T1D. Dec. at 62-63.[4] And so, the record evidence shows that any inconsistency in the statements of the special master regarding the extent of petitioner's pre-vaccination control of her T1D had no bearing upon the special master's ultimate determination

[4] The special master found that there was no medical record proof that petitioner experienced a reaction to the first HPV dose prior to her October 2014 hospital visit, to corroborate the argument that the HPV vaccine is responsible for the worsening of her T1D. Dec. at 63. The special master also found that no treaters who saw petitioner at any time close to the date of her first HPV vaccination on July 15, 2014, opined that there could be a relationship between the vaccine and petitioner's T1D flares. *Id.* The special master similarly found a lack of evidence of any symptoms during the weeks following petitioner's vaccinations on August 19, 2015. *Id.* at 63-64. And so, he concluded that petitioner had not shown that these vaccines significantly aggravated her T1D. *Id.* at 64.

that petitioner had not shown that any of the vaccines at issue could have, and in fact did, worsen her T1D.

B. The Special Master Did Not Err By Considering Petitioner's Behavior During Adolescence

Petitioner's argument that the special master abused his discretion by considering evidence regarding her behavior during late adolescence is also unsubstantiated by the record evidence. Petitioner argues that the special master erred by considering evidence regarding "a single instance of self-reported intoxication" during college and the opinion of the Secretary's expert, Dr. MacGinnitie, that the attendant life changes that occur at the college level could have caused the worsening of petitioner's T1D. Pet'r Mem. at 19. Again, a careful review of the November 13, 2020, Decision and the record evidence in this case show that the special master appropriately considered and weighed this evidence.

First, the special master appropriately considered evidence in the medical record regarding petitioner's behavior during her college years. The special master correctly observes in the November 13, 2020, Decision that the medical record contains "direct instances" where petitioner acknowledged the role of her own conduct in contributing to her T1D flares during late adolescence. Dec. at 63 (citing Pet'r Ex. 31 at 122) (providing that on April 21, 2017, petitioner visited the ER with the chief complaint of intoxication and reports of repetitive vomiting). Petitioner does not dispute this evidence. *See* Pet'r Mem. at 19-20. And so, petitioner provides no basis for the special master to have disregarded this evidence.

The record evidence also shows that the special master appropriately considered and weighed the expert opinion of Dr. MacGinnitie in analyzing petitioner's significant aggravation claim. In the November 13, 2020, Decision, the special master states that he was persuaded by Dr. MacGinnitie's opinion that the deterioration of diabetes control that petitioner experienced in this case is often seen during late adolescence. Dec. at 63. The Federal Circuit has held that a special master may consider the evidence presented by the Secretary in determining whether the petitioner has established a *prima facie* case of causation. *See Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); *de*

Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case[-]in-chief."). And so, in this case, the special master appropriately considered Dr. MacGinnitie's expert opinion in analyzing petitioner's significant aggravation claim. Dec. at 63.

It is also important to note that while the special master determined that the aforementioned evidence diminished petitioner's evidence of causation, he also concluded that the evidence suggesting that petitioner's behavior during late adolescence contributed to the worsening of her T1D was not established to a sufficient degree to make a formal "factor unrelated" finding. *Id.* And so, the special master did not abuse his discretion in considering and weighing evidence regarding petitioner's behavior during late adolescence in analyzing her significant aggravation claim.

C. The Special Master Appropriately Analyzed Petitioner's SFN Diagnosis

Petitioner also has not shown that the special master abused his discretion by considering the opinion of the Secretary's expert, Dr. Christopher Gibbons, with regards to her SFN diagnosis. Petitioner correctly observes in her motion for review that the special master determined that Dr. Gibbons raised "reasonable points about the evidentiary strength" of her SFN diagnosis and that the special master also found that several of petitioner's other alleged injuries were not preponderantly established. Dec. at 52-54, 59. But, a careful review of the record evidence makes clear that the special master did not abuse his discretion in making these determinations, because he properly analyzed petitioner's claim that the HPV vaccine caused her SFN under *Althen*.

In this regard, a careful review of the November 13, 2020, Decision shows that the special master analyzed petitioner's medical theory of causation with respect to her SFN diagnosis under *Althen* prong 1, despite his concerns that the medical record did not support this diagnosis. Notably, the special master states in his decision that "even if [he] assume[s] . . . that [petitioner's SFN] diagnosis has reliable/substantive medical support," petitioner's claim that the HPV vaccine could cause SFN had not been "reliably established." *Id*. at 59.

The record evidence also shows that the special master's determination that petitioner failed to make a preponderant showing that the HPV vaccine can cause SFN is supported by

substantial evidence. *Id*. at 59-60. Specifically, the special master determined that Dr. Steinman's expert opinion and the BLAST search results upon which he relied were not sufficient to show a link between the HPV vaccine and SFN. *Id.* at 59. The special master also determined that petitioner failed to corroborate her medical theory that the HPV vaccine can produce antibodies that will cross-react against human nerve cells with other reliable evidence. *Id.* The special master similarly analyzed petitioner's medical theory with regards to her POTS, narcolepsy and CFS diagnoses under the first prong of *Althen*, and he reasonably concluded that petitioner had not established that the HPV vaccine could cause any of these conditions with reliable scientific evidence. *Id*. at 56-59.[5] Because the special master's determinations regarding petitioner's SFN diagnosis are supported by the substantial evidence in this case, the Court will not set aside the determinations of the special master.

D. The Special Master Reasonably Concluded That Petitioner Failed To Establish That The HPV Vaccine Caused Her CFS

Petitioner's argument that the special master arbitrarily determined that there is no link between the HPV vaccine and her CFS is equally unavailing. Petitioner argues that the special master arbitrarily determined that there was no link between the HPV vaccine and CFS, because the cause of fatigue and sleep disorders is not well understood. Pet'r Mem. at 21. Given this, petitioner maintains that she has established all three *Althen* prongs with regards to her CFS diagnosis in this case. *Id.* at 22. The record evidence shows, however, that the special master reasonably concluded that petitioner did not satisfy the three prongs of *Althen* with regard to her claim that the HPV vaccine caused her CFS for several reasons.[6]

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[5] Petitioner correctly observes that the special master suggested that the medical record in this case might support a diagnosis of diabetic neuropathy. Pet'r Mem. at 20; Dec. at 59, n.77. But, the record evidence makes clear that this suggestion had no impact on the special master's analysis of petitioner's claim that the HPV vaccine caused her SFN. *See* Dec. at 59-60. Petitioner's objection that the special master afforded more weight to the opinion of Dr. Gibbons than to her treating physicians also lacks merit. Pet'r Mem. at 20. The special master is not bound by a treating physician's conclusions. *Snyder ex rel. Snyder v. Sec'y of Health and Hum. Servs*., 88 Fed. Cl. 706, 746, n.67 (2009).

[6] The Court assesses the special master's determination that petitioner failed to satisfy *Althen* with regards to her CFS diagnosis by considering whether that determination is supported by the substantial evidence. *Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1355, 1363 (citation omitted) (holding that a special master's findings regarding the probative value of the evidence and the credibility of witnesses will not be disturbed so long as they are "supported by substantial evidence").

1. Petitioner Has Not Established A Medical Theory

First, the record evidence shows that petitioner's evidence to support her medical theory that the HPV vaccine can cause CFS is insufficient to satisfy the preponderance of the evidence standard in Vaccine Act cases. *See Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (quoting *Knudsen by Knudsen v. Sec'y of Dep't of Health & Hum. Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994)). As the special master observes in the November 13, 2020, Decision, petitioner can satisfy the first *Althen* prong without resorting to medical literature, epidemiological studies, a demonstration of a specific mechanism or a generally accepted medical theory. Dec. at 45; *see also Andreu ex rel. Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378 (Fed. Cir. 2009) (quoting *Capizzano v. Sec'y of Health & Hum. Servs.* 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). But, the first prong of *Althen* is not satisfied by merely establishing the proposed causal theory's scientific or medical plausibility. *See Boatmon*, 941 F.3d at 1360; Dec. at 45. And so, petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the [Court] of the fact's existence." *Moberly v Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (brackets existing) (citations omitted); *see also Snowbank Enters., Inc. v. United States*, 6 Cl. Ct. 476, 486 (1984) (holding that mere conjecture or speculation is insufficient under a preponderance standard); *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005) (citing *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

In this case, the record evidence shows that the special master's conclusion that petitioner failed to establish a scientifically reliable medical theory of causation with regards to her CFS diagnosis is supported by substantial evidence. To support her medical theory that specific homologies between HPV protein fragments and M3 and M4 muscarinic receptors can trigger "clinically relevant neuroinflammation" associated with CFS, petitioner relies upon the expert testimony of Dr. Steinman, certain BLAST search results and several medical articles and case studies, including the *Blitshteyn*, *Loebel* and *Ikeda* studies. Pet'r Mem. at 22; *see also* Pet'r Ex. 86 at 24, 26-27; Pet'r Ex. 96 at 4 (*Blitshteyn* study noting elevated muscarinic receptor 3 and 4 antibodies have been found in CFS patients); Pet'r Ex. 97 at 1 (*Loebel* study noting that antibodies against M3 and M4 receptors were significantly elevated in CFS patients compared to

controls); Pet'r Ex. 107 at 4 (*Ikeda* study noting that the autoantibodies against the adrenergic receptor β2 and muscarinic acetycholine receptor 3 and 4 were significantly elevated in the serum of patients with CFS). But, a careful review of the case studies upon which petitioner relies shows that these studies cast some doubt upon her medical theory that the HPV vaccine can produce antibodies that play a role in the pathogenesis of CFS. For example, the *Blitshteyn* case study notes that the autoimmunity and autoantibodies that petitioner cites to link the HPV vaccine to CFS have only been found in a subset of CFS patients in "preliminary studies in small groups of patients." *See* Pet'r Ex. 96 at 4. The *Loebel* study similarly questions petitioner's medical theory, because this study also finds elevated levels of antibodies in only a subset of CFS patients. Pet'r Ex. 97 at 7. Perhaps more significantly, the *Ikeda* study acknowledges that there is no significant association between major CFS symptoms and antibodies. *See* Pet'r Ex. 107 at 4. And so, the case studies that petitioner relies upon in this case raise questions about the reliability of her medical theory.

In addition, as the special master correctly observes in the November 13, 2020, Decision, evidence of a link between CFS and the HPV vaccine is rebutted by other medical and scientific evidence found in the record for this case. Dec. at 59. For example, the *Chao* study notes that no autoimmune signals were found after test subjects received the HPV vaccine. *See* Resp't Ex. C, Tab 18 at 1, 9. The *Barboi* study also finds no data to support a causal relationship between the HPV vaccination and chronic fatigue. Resp't Ex. M at 1. In addition, the *Suzuki* study similarly finds no causal association between the HPV vaccine and fatigue.[7] Resp't Ex. L at 1, 8. Given this evidence, the special master reasonably concluded that petitioner failed to satisfy the first prong of *Althen* based upon a preponderance of the evidence. *Lonergan v. Sec'y of Dep't of Health & Hum. Servs.*, 27 Fed. Cl. 579, 579-80 (1993) (holding that the Court will not substitute its judgment for that of the special master "if the special master has considered all relevant factors, and has made no clear error of judgment.").[8]

[7] Dr. Raizen's second expert report notes that scientifically reliable studies, such as the *Feiring* and *Donegan* studies, have similarly not found an association between the HPV vaccine and CFS. Resp't Ex I at 5 (citing Resp't Ex. I, Tabs 5-6).

[8] Petitioner's argument that the special master improperly heightened her burden of proof, by dismissing evidence that she provided to establish homologies between the HPV vaccine amnio acid sequences and human nerve cells, is also unpersuasive. Pet'r Mem. at 21. As discussed above, the record evidence shows that the special master appropriately analyzed petitioner's theory of causation under the first prong

2. Petitioner Has Not Established A Logical Sequence

Second, a careful review of the record evidence also shows that petitioner has not established a logical sequence of cause and effect showing that the HPV vaccine was the reason for her CFS diagnosis. *Althen*, 418 F.3d at 1278. Petitioner maintains that she has satisfied the second prong of *Althen*, because she has been tested with elevated results for certain antibodies that are found in some individuals with CFS and that have been found to be related to "post HPV vaccination disorders." Pet'r Mem. at 22. But, as discussed above, the special master carefully considered the evidence offered by petitioner to establish that her elevated levels of muscarinic antibodies played a significant role in the pathogenesis of CFS and he reasonably concluded that petitioner had not established that such a connection exists. Dec. at 9 n.24, 17, 59. And so, the Court will not disturb the decision of the special master.

3. Petitioner Has Not Established A Proximate Temporal Relationship

Lastly, petitioner has not established a proximate temporal relationship between her HPV vaccinations and the onset of her CFS symptoms under the third prong of *Althen*. *Althen*, 418 F.3d at 1278. To satisfy this prong of *Althen*, petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically[-]acceptable to infer causation-in-fact." *de Bazan*, 539 F.3d at 1352 (citation omitted). As the special master correctly observes in the November 13, 2020, Decision, the temporal relationship between petitioner's CFS diagnosis and the vaccinations at issue is too remote to establish a proximate temporal relationship. Dec. at 60-61. Notably, the record evidence shows that petitioner was diagnosed with CFS in August 2018—approximately

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of *Althen* and reasonably concluded that petitioner failed to make a preponderant showing that the HPV vaccine can cause CFS. Dec. at 58-59. As also discussed above, the record evidence also makes clear that the special master acknowledged that petitioner offered some evidentiary support to establish a link between the HPV vaccine and CFS, but he found this evidence insufficient. *Id.* at 18, 58-59. And so, the challenge for petitioner in this case is not that the special master heightened her burden of proof, but rather that the evidence to support her medical theory is not sufficient or reliable enough to satisfy the preponderance of the evidence standard under *Althen*. *See* Dec. at 59 (determining that "merely showing via BLAST searches that some homology exists between amino acid sequences in the HPV vaccine components and nerve cells does not amount to a preponderant showing that the vaccine can produce antibodies that will cross-react against those cells.").

three years after she received the second dose of the HPV vaccine. *Compare* Pet'r Ex. 3 at 6 *with* Pet'r Ex. 98 at 26. Petitioner has not provided evidence to show that the onset of her CFS symptoms occurred within a medically-acceptable timeframe.[9] And so, the special master's conclusion that petitioner has not satisfied the third prong of *Althen* with regards to her CFS diagnosis is also supported by substantial evidence and should not be set aside.

E. The Special Master Appropriately Considered Relevant Case Law

As a final matter, the record evidence in this case also makes clear that the special master appropriately considered relevant case law in analyzing petitioner's vaccine injury claim. In the November 13, 2020, Decision, the special master makes reference to several prior cases before the Office of Special Masters declining to find a link between vaccines and T1D. Dec. at 62 (observing that "it has repeatedly been determined in [Vaccine Act] cases that vaccination does not likely worsen [T1D].") (citing *Hennessey v. Sec'y of Health & Hum. Servs.*, No. 01-190V, 2009 WL 1709053 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for rev. den'd*, 91 Fed. Cl. 126 (2010)). But, the special master also correctly recognizes in his decision that "[a] prior decision in different cases [does] not *control* the outcome herein." Dec. at 51 (emphasis in original) (citing *Boatmon*, 941 F.3d at 1358-59).

The record evidence also shows that the special master appropriately relied upon prior cases in determining that "it is far from certain that small fiber neuropathy *is* an autoimmune-driven condition." *Id.* at 59 (emphasis in original) (citing *Todd v. Sec'y of Health & Hum. Servs*., No. 15-860V, 2020 WL 727973, at *21 (Fed. Cl. Spec. Mstr. Jan. 8, 2020)). Again, the record evidence shows that the special master appropriately analyzed petitioner's claim that the HPV vaccine could cause SFN consistent with *Althen*, notwithstanding his concerns about whether SFN is in fact an autoimmune driven condition. *Id.* at 59-60. Given this, petitioner's final objection to special master's decision is unsubstantiated by the record evidence in this case.

[9] Petitioner relies upon an observational study from Japan which finds that certain symptoms, including fatigue, headache, sleep disturbance, and autonomic dysfunction, manifested on average within 360 days of the subject receiving the HPV vaccine. Pet'r Ex. 100. But, petitioner's CFS diagnosis occurred almost three years after vaccination.

V. CONCLUSION

In sum, the record evidence in this Vaccine Act case shows that the special master reasonably determined that petitioner had not established that any of the vaccines that she received on July 15, 2014, and August 15, 2015, significantly aggravated her T1D, or caused her headaches, POTS, SFN, CFS or narcolepsy, based upon a preponderance of the evidence in this case. While petitioner's case is a difficult one, given the clear evidence in the medical record showing the worsening of her T1D and her struggles with many other symptoms post-vaccination, the special master's decision to deny compensation is supported by substantial evidence and consistent with the Vaccine Act. And so, for the forgoing reasons, the Court:

1. **DENIES** petitioner's motion for review of the special master's November 13, 2020, Decision; and

2. **SUSTAINS** the decision of the special master.

The Clerk shall enter judgment accordingly.

Some of the information contained in this Memorandum Opinion and Order may be considered privileged, confidential or sensitive personally-identifiable information that should be protected from disclosure. And so, this Memorandum Opinion and Order shall be **FILED UNDER SEAL**. The parties shall review the Memorandum Opinion and Order to determine whether, in their view, any information should be redacted prior to publication. The parties shall also **FILE**, by **June 7, 2021**, a joint status report identifying the information, if any, that they contend should be redacted, together with an explanation of the basis for each proposed redaction.

IT IS SO ORDERED.

s/ Lydia Kay Griggsby
LYDIA KAY GRIGGSBY
Judge